Perchlorate Data Gaps

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Original Database

Human Studies

- Graves disease patients
- Healthy volunteers

Animal Studies

- Less than 90 days
- Cancer bioassays
- Limited developmental/reproductive

Original Data Gaps

Studies needed to complete database:

- at least subchronic bioassay
- two-generation reproductive study
- developmental toxicity studies in two species

Studies to identify critical effect or reduce uncertainty:

- developmental neurotoxicity study
- genotoxicity study
- immunotoxicity study

Other major unanswered questions:

- shape of dose-response curve in humans
- effects from long-term exposure
- effects in organs/systems other than thyroid
- more complete understanding of kinetics and mechanism

First Round of Studies

- 90-day subchronic oral bioassay
- Two-generation reproductive toxicity
- Developmental toxicity in one species
- Neurobehavioral developmental
- Genotoxicity
- Immunotoxicity
- PBPK

Remaining Data Gaps

Studies needed to complete database:

- developmental toxicity studies in a second species

Studies to identify critical effect or reduce uncertainty:

- establish separate dose-response curves for thyroid hypertrophy and hyperplasia
- predictive immunotoxicity study

Other major unanswered questions:

- If dam is hypothyroid at time of conception, what are effects on fetal/neonatal thyroid and neurological development?
- Is perchlorate transferred to pup via milk?
- How do serum hormone levels correlate with thyroid pathology and neurohistopathology (fetal only)?

- What is the effect of perchlorate on fetal/neonatal mental development?
- What is shape of dose-response curve in humans?

Second Round of Studies

- PWG reevaluation of all thyroid histopathology
- Predictive immunotoxicity studies
- Developmental toxicity study in rats
- “Effects study”
- Motor activity study
- Epidemiology and clinical human studies
- PBPK modeling

Remaining Data Gaps

Studies needed to complete database:

- none

Studies to identify critical effect or reduce uncertainty:

- host resistance assay
- explore use of data-derived uncertainty factors following IPCS guidelines

Other major unanswered questions:

- How do we better integrate the existing human and animal data?
- How do thyroid hormones fluctuate over time in animals and how do we explain some seemingly inconsistent findings in the animal studies?

- How do we define the breakdown of normal thyroid homeostasis and progression to adversity?
- Have we established dose-response curves for this process?

Information and Status of Perchlorate Studies

http://www.tera.org/perchlorate